TOBACCO INDUSTRY RESEARCH COMMITTEE
350 FIFTH AVENUE NEW YORK 1, N.Y.

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Application For Research Grant

Date: September 26, 1955

1. Name of Investigator: Dr. John L. Patterson, Jr.
Dr. Wyndham B. Blanton, Jr.

2. Title: Associate Professor of Medicine, MCV
Assistant to the Dean MCV } Co-investigators

3. Institution & Address: Medical College of Virginia,
1200 East Broad Street,
Richmond 19, Virginia.

4. Project or Subject: Detection and Prognostic Significance of Early Obstructive Pulmonary Disease.

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5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

Introductory Remarks:

The most common and incapacitating form of chronic pulmonary disease of the later years is chronic pulmonary emphysema. The view usually advanced regarding its pathogenesis centers about the effect of long standing and progressive airway obstruction, bronchiolar obstruction being considered the most important because of the high airflow resistance in small tubes. Most of the reported studies on the pathological ~~xxx~~ physiology of this disease have been concerned with the stages in which definite clinical symptoms and signs are recognizable, i.e. usually moderate to far advanced disease.

In light of present knowledge of the pathology of advanced pulmonary emphysema, it is reasonable to assume that the only effective way of combating the later disability is via prophylactic or very early therapeutic measures. To apply such methods will necessitate the identification of individuals with early obstructive disease. The proposed investigations were conceived under the hypothesis that with proper methods it should be possible to detect early, perhaps definitely pre-clinical, degrees of bronchiolar obstruction.

In order to test the validity of this hypothesis, it would appear desirable, at least in the initial studies, to make observations on a ~~xx~~ group of subjects whose bronchial and bronchiolar involvement might be improved in a high percentage of cases. Subject groups for consideration are moderate to heavy users of tobacco before and after cessation of smoking, patients with allergic bronchitis, patients with reversible chronic infectious bronchitis and individuals whose occupations subject them to the inhalation of irritant gases. The group of chronic smokers would seem to be the most favorable group for immediate study, since they offer

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the most readily controlled means of alleviating the bronchitis by cessation of smoking.

Plan of Procedure:

The common methods of pulmonary function study in most cases do not appear applicable to the problem of detection of minimal bronchiolar obstruction. A possible exception to this is the well-known Maximum Breathing Capacity, although the significance of small changes in this measurement are difficult to evaluate and its usefulness in this type of study is doubtful. A reasonable approach would be to place the airway system under maximal stress by having the individual carry out maximal expiratory and inspiratory effort during which airway resistance would be studied. One measure of this resistance can be obtained by continuously recording the trans-pulmonary pressure gradient, i.e. the gradient from the surface of the lung to the mouth, together with simultaneous recording of instantaneous velocity of airflow during the expiratory effort. It is proposed to measure velocity of airflow by means of a screen type of flowmeter of sufficient diameter to permit linearity of response up to 600 liters per minute. Intrathoracic pressure, or an approximation to it, can be obtained from a small diameter esophageal balloon.(1) It is felt that under the conditions of this experiment, i.e. maximal expulsive effort, the admitted error due to esophageal tone (noted in quiet breathing) should not seriously affect the results in view of the total pressure being measured. Since resistance to airflow with laminar flow tends to be proportional to velocity of flow, whereas resistance in the case of turbulent flow is proportional to the square of the velocity, the method described above should be particularly sensitive in the detection of small decreases in airway caliber if these are associated with increased turbulence. The type of pathologic changes which we believe occur in the tracheobronchial tree in the conditions to be studied leads us to anticipate increase in turbulent flow.

The equipment will be designed for simultaneous use with more simple apparatus for measurement of respiratory function so that the possible utility of the latter in detection of early obstructive disease can be evaluated. There has been developed in this laboratory a simple type of recording spirometer with minimal friction and inertia properties which, it is hoped, will prove useful for this purpose.

A somewhat different approach to the detection of early bronchiolar obstruction is the measurement of the effects of such obstruction on the equality of inequality of distribution of inspired air throughout the lung. Techniques are available at present for measuring defective intra-pulmonary gas mixing by the continuous analysis of helium concentration in expired gas after equilibration of the subject on a helium&oxygen mixture.(2) or of expired nitrogen concentration after a single breath of 100% oxygen.(3) The sensitivity of both the nitrogen and helium methods leads us to anticipate detectable changes in these measures of pulmonary air distribution in the presence of early sub-clinical airway obstruction.

It is planned to correlate the findings determined by resistance, air distribution, and simple respirometer methods.

The plan of procedure is as follows: Control studies on given subjects will be done repetitively for consistency of findings after detailed clinical examination. When these are completed, the measure designed to diminish or relieve the bronchiolar obstruction, for example, cessation of smoking, will be instituted followed by serial studies at appropriate intervals until maximal change has been achieved. The attempt will then be made in some subjects to restore the original status, which would involve, in the example cited, reinstitution of smoking and again a series of experimental studies. The number of subjects required for the study will depend upon the consistency of the findings and cannot be estimated with certainty, but a working figure of twenty subjects appears reasonable.

No chest colds of inflammation
Prob 1st cig after rest will be different

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1. Mead, J., McIlroy, M.D., Selverstone, N. J., and Kriete, B. C., Measurement of Intraesophageal Pressure, Journal of Applied Physiology, 7:491,1955.

2. Blair, E. and Hickam, J.B., Quantitative Study of Intrapulmonary Gas Mixing in Emphysema, American Journal of Medicine, 18:519, 1955.

3. Comroe, J. H. and Fowler, W. S., Lung Function Studies: VI. Detection of Uneven Alveolar Ventilation during a Single Breath of Oxygen, American Journal of Medicine, 10:408, 1951.

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Source: https://www.industrydocuments.ucsf.edu/docs/fnvn0000

6. Budget Plan:

Salaries	$1,380.00
Expendable Supplies	618.04
Permanent Equipment	2,815.00*
Overhead	886.96
Other	1,100.00**
Total	$6,800.00

7. Anticipated Duration of Work: One Year.

8. Facilities and Staff Available:

The facilities of the Pulmonary Function Laboratory of the Medical College of Virginia are available to this project. The plan calls for assighment of approximately one-half the time of a qualified technician to work solely with this project, under the supervisioh of the investigators named above.

9. Additional Requirements:

None.

10. Additional Information (Including relation of work to other projects and other sources of supply):

This work will be carried out in the facilities of the Medical College of Virginia Pulmonary Laboratory which operates in close conjunction with the Cardiovascular Research Laboratories. At the present time a number of other investigative studies in the field of cardio-respiratory physiology are being carried out by these groups and the advice of and, to some extent, the time of the personnel involved will be available as necessary.

*Permanent Equipment:

Flowmeter:	
Differential Strain Gauge	$350.00
Differential Strain Gauge Amplifier	350.00
Screen and Housing	100.00
Nitrogen Meter (The Waters Corp.)	1,675.00
Helium Kathorometer (Gow-Mac Instrument Corp.) With Housing	70.00
Leeds-Northrup Potentiometer double acale range 0-16 and 16-64 m.volts	270.00

**Other:

Paid Subjects	$800.00
Cost of X-ray	300.00

s/ W. B. Blanton, Jr.

Signature s/ John L. Patterson, Jr.
Director of Project

s/ W. F. Tompkins
Business Officer of the Institution
W. F. Tompkins

Source: https://www.industrydocuments.ucsf.edu/docs/wwdd0000

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